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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,477	02/04/2002	Shuji Hinuma	70342/47147CPA-C	8361

21874 7590 02/11/2004

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EXAMINER	
ULM, JOHN D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,477	HINUMA ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/17/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *5-10,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☒ Claim(s) *11-13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/796,570.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/04/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 15 are pending in the instant application.

2) Claims 5 to 10, 14 and 15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made without traverse in the correspondence filed 17 November of 2003.

3) Claims 2 to 4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A properly dependent claim can not be conceivably be infringed without infringing the claims from which it depends. Claims 2 to 4 are improperly dependant from claim 1 because they can be infringed without infringing claim 1.

4) Claims 11 to 13 are objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim must depend from other claims in the alternative only. Each of these claims encompasses an embodiment that depends from claim 1 and claim 2. See M.P.E.P. § 608.01(n). According, claims 11 to 13 have not been further treated on the merits.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5) Claims 1 to 4 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The instant claims encompass a protein and fragments thereof as they occur in nature. Because all proteins are

degraded and replaced during the course of cellular metabolism a cell which produces a protein of the instant invention also produces fragments thereof.

6) Claims 1 to 4 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect. It is clear from the instant specification that the receptor protein described therein as "a novel human amygdaloid nucleus-derived g protein coupled receptor" is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it

appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", A [u]nless and until a process is refined and developed to this point" "where specific benefit exists in currently available form" "there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion the a protein of the instant invention will bind to any one of the plurality of structurally unrelated compounds that are listed on page 8 of the instant specification. Until some actual and specific significance can be attributed to a protein comprising the amino acid sequence presented in SEQ ID NO:1 of the instant application, or the gene encoding it, the instant invention is incomplete. The protein of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as G protein-coupled receptors. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for a protein comprising the amino acid sequence presented in SEQ ID NO:1 of the instant application then the claimed invention is

incomplete and, therefore, does not meet the requirements of 35 U.S.C. ' 101 as being useful.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7) Claims 1 to 4 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

8) Claims 1 to 4 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making a functional protein comprising the entire amino acid sequence presented in SEQ ID NO:1 of the instant application and non-functional fragments thereof which are at least 16 amino acids in length, does not reasonably provide enablement for the production of a functional protein lacking that sequence or for the production of a functional fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The instant specification describes a single protein having a specific amino acid sequence. This is a naturally occurring protein whose identification as a receptor protein is based solely upon its presumed structurally similarity to known G protein-coupled receptors. Because this protein occurs in nature, a practitioner would reasonably conclude that it is a functional receptor protein.

The instant claims, however, are not limited to the single naturally occurring protein which is disclosed in the instant specification. They also encompass a protein whose amino acid sequence is "a substantial equivalent" to that disclosed sequence, and partial peptides thereof. Because the instant specification does not identify a ligand for the disclosed protein or a functional assay therefore, it is not possible for an artisan to determine if an altered protein is substantially equivalent to the disclosed protein or not. Further, because the instant specification does not identify those amino acid residues in the amino acid sequence SEQ ID NO:1 which are essential for the biological activity and structural integrity of that protein and those residues which are either expendable or substitutable, even if a functionality assay were available a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 400 amino acid residues before they could even begin to rationally design a substantially equivalent protein having other than a natural amino acid sequence. The disclosure of a single DNA sequence encoding a single putative G protein-coupled receptor with a natural amino acid sequence is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass any and all substantially equivalent proteins or functional fragments thereof.

The current claim limitations are analogous to those of claim 7 of U.S. Patent Number 4,703,008 which were held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement in Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016 (see page 1026, section D). In that instance, a claim to a nucleic acid

encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. §112, first paragraph, for want of enablement. This limitation is analogous to the "substantial equivalent" limitation of the instant claims. The disclosure upon which that claim was based described a recombinant DNA encoding EPO and a few analogs thereof. That disclosure differs from the instant specification because, whereas the instant specification describes a DNA encoding putative G protein-coupled receptor, it does not describe even a single equivalent thereof. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify the grant of the claims sought. As indicated, the instant specification is even more limited than the '008 patent because it describes only a single protein and no analogs or mutants thereof and, therefore, provides even less support than the '008 specification for claims of comparable scope and which were held to be invalid in that patent.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9) Claims 1 to 4 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9.1) Claim 1 is vague and indefinite because one can not determine which subject matter is included and excluded by the term "substantial equivalent thereto". Claims 2 to 4 are vague and indefinite in so far as they depend from claim 1 for this element.

9.2) Claim 2 is confusing because of the term "except for SEQ ID NO:3 or fragments thereof". If Applicant wishes to claim a polypeptide comprising less than all of the amino acid sequence presented in SEQ ID NO:1 then this is what they should claim. If Applicant wishes to exclude certain regions of SEQ ID NO:1 from the claimed polypeptides then they should refer to those portions of SEQ ID NO:1 which are to be excluded. As this claim is currently written it does not comply with 37 C.F.R. § 1.822(o) which requires a separate sequence listing for any sequence which is made up of one or more noncontiguous segments of a larger sequence. Claim 3, for example, should be directed to "a polypeptide consisting of at least 16 contiguous amino acid residues from amino acid ## to amino acid ## or amino acid ## to amino acid ## of SEQ ID NO:1". Claims 3 and 4 are vague and indefinite in so far as they depend from claim 2 for this element.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10) Claims 1 to 4 are rejected under 35 U.S.C. § 102(b) as being anticipated by the Harrigan et al. publication (Mol. Endocrinol. 5(9):1331-1338, 1991, cited by

Applicant). Figure 3 on page 1335 of the Harrigan et al. publication described a murine protein whose amino acid sequence is 89% identical to the human amino acid sequence presented in SEQ ID NO:1 of the instant application. An artisan would reasonably conclude that the amino acid sequence of the protein described by Harrigan et al. is "a substantial equivalent" of the sequence presented in SEQ ID NO:1 of the instant application. The description of the entire amino acid sequence of a protein inherently constitutes a description of any and all fragments thereof.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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